

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claim 1. (Currently Amended) A method for preparing a recombinant minimal adenoviral vector stock comprising:

- (a) Introducing in a first cell line (i) a first helper adenoviral vector or virus and
 - (ii) a second helper adenoviral vector or virus, the genome genomes of both (i) and (ii) comprising 5' and 3' ITRs, an encapsidation region and one or more gene(s) of the early and late regions, and the genome of (ii) comprising 5' and 3' ITRs, an encapsidation region and one or more gene(s) of the early and late regions,
- wherein the genome of (i) is obtained from a first adenovirus genome,
- wherein the genome of (ii) is obtained from a second adenovirus genome with the exception of at least the encapsidation region which is obtained from said first adenovirus genome,
- wherein said first helper (i) is capable of packaging said second helper (ii) in said first cell line; and

- wherein said first adenovirus genome is an animal adenovirus genome and said second adenovirus genome is a human adenovirus genome;
- (b) culturing the first cell line generated following step (a) ~~the cell obtained in step (a)~~ under appropriate conditions to allow the production of viral particles comprising (ii)
- (c) recovering the viral particles obtained in step (b) from the cell culture,
- (d) introducing in a second cell line said viral particles obtained in step (c) and a recombinant minimal vector which is defective for all adenoviral genes,
- (e) culturing the second cell line generated following step (e) ~~the cell obtained in step (d)~~ under appropriate conditions to allow the production of viral particles comprising said recombinant minimal vector which is defective for all adenoviral genes, and
- (f) recovering the viral particles obtained in step (e) from the cell culture.

Claim 2. (Canceled)

Claim 3. (Previously Presented) The method of claim 1, wherein said first adenovirus genome is a bovine adenovirus genome and said second adenovirus genome is a human adenovirus genome.

Claim 4. (Previously Presented) The method of claim 3, wherein said first adenovirus genome is a BAV3 genome and said second adenovirus genome is an Ad5 genome.

Claim 5. (Canceled)

Claim 6. (Currently Amended) The method of claim 1, wherein said first helper (i) or said second helper (ii) or ~~and~~ said first helper (i) and said second helper (ii) is (are) a defective mutant(s) of a wild-type adenovirus genome.

Claim 7. (Previously Presented) The method of claim 6, wherein said first and second helpers (i) and (ii) are defective mutants of wild-type adenovirus genomes and are capable of cross-complementing each other for at least one defective function.

Claim 8. (Previously Presented) The method of claim 6, wherein said first helper (i) is defective for E1 function.

Claim 9. (Previously Presented) The method of claim 6, wherein said first helper (i) is defective for E2 function.

Claim 10. (Previously Presented) The method of claim 9, wherein said defective E2 function is caused by a mutation or deletion in one or more of the genes selected from the group consisting of the genes encoding DBP, Pol and pTP.

Claim 11. (Previously Presented) The method of claim 6, wherein said second helper (ii) is defective for E1 function.

Claim 12. (Currently Amended) The method of claim 11, wherein said second helper (ii) ~~vector~~ is an Ad5 genome deleted of nucleotides approximately 455 to approximately 3327 and having nucleotides approximately 149 to approximately 454 comprising the Ad5 encapsidation region replaced by nucleotides approximately 141 to approximately 984 of the BAV3 genome.

Claim 13. (Currently Amended) The method of claim 1, wherein said second helper (ii) is functional for the E1 function and contains an E1 region providing all said E1 functions ~~function~~ placed under the control of a non-adenoviral vector promoter.

Claim 14. (Previously Presented) The method of claim 1, wherein said first and second helpers (i) and (ii) have an origin of replication recognized by the same E2-encoded gene products.

Claim 15. (Currently Amended) The method of claim 14, wherein the endogenous 5' and 3' ITRs of the first helper (i) are modified to enable make the origin of replication to be recognized by the E2 gene products expressed from the second helper (ii).

Claim 16. (Currently Amended) The method of claim 15, wherein said modification consists in the replacement of:

- the penultimate 20 bp containing the core origin,
- the penultimate 50 bp containing the entire origin of replication or
- the entire ITRs

of said first helper (i) with ~~by~~:

- the penultimate 20bp containing the core origin
- the penultimate 50bp containing the entire origin of replication, or
- the entire ITRs

of the 5' and 3' ITRs of said second helper (ii).

Claim 17. (Currently Amended) The method of claim 14, wherein the endogenous 5' and 3' ITRs of the second helper (ii) are modified to enable ~~make~~ the origin of replication to be recognized by the E2 gene products expressed from the first helper (i).

Claim 18. (Previously Presented) The method of claim 17, wherein the endogenous 5' and 3' ITRs of said second helper (ii) are replaced by the 5' and 3' ITRs of said first adenovirus genome.

Claim 19. (Previously Presented) The method of claim 18, wherein said second helper (ii) is an Ad5 genome deleted of nucleotides approximately 455 to approximately 3327 and nucleotides approximately 28592 to approximately 30470 and having nucleotides approximately 1 to approximately 454 comprising the 5' ITR

and the Ad5 encapsidation region replaced by nucleotides approximately 1 to approximately 984 of the BAV3 genome and nucleotides approximately 35826 to approximately 35935 comprising the 3' ITR replaced by nucleotides approximately 34188 to approximately 34446 of the BAV3 genome.

Claim 20. (Previously Presented) The method of claim 1, wherein said first cell line is a non-human cell line.

Claim 21. (Previously Presented) The method of claim 20, wherein said first cell line has a bovine origin and wherein said first helper (i) is obtained from a BAV 3 genome.

Claim 22. (Previously Presented) The method of claim 20, wherein said first cell line is capable of complementing part of all of at least one defective function of a helper vector selected from the group consisting of the first helper (i), the second helper (ii) and the first and second helpers (i) and (ii).

Claim 23. (Previously Presented) The method of claim 22, wherein said first cell line complements the E1 function of a helper vector selected from the group consisting of the first helper (i), the second helper (ii) and the first and second helpers (i) and (ii).

Claim 24. (Previously Presented) The method of claim 1 wherein said second cell line is of human origin.

Claim 25. (Previously Presented) The method of claim 24 wherein said second cell line is capable of complementing part of all of at least one defective function of said recombinant minimal vector.

Claim 26. (Previously Presented) The method of claim 25, wherein said second cell line is a complementing cell line for Ad5 E1 function.

Claim 27. (Original) The method of claim 26, wherein said second cell line is selected among the group consisting of PER-C6 and 293.

Claim 28. (Previously Presented) The method of claim 1, which comprises an additional step following step (f), wherein said viral particles recovered in step (f) are used to reinfect said second cell line in the presence of an additional quantity of second helper (ii).

Claim 29. (Previously Presented) The method of claim 1, which further comprises a purification step of the viral particles obtained in step (f).

Claim 30. (Previously Presented) The method of claim 1, wherein said viral particles obtained in step (f) are helper-free.

Claim 31. (Withdrawn) An animal adenovirus genome having modified 5' and 3' ITRs and wherein said modification consists in the replacement of:

- the penultimate 20 bp containing the core origin,
- the penultimate 50 bp containing the entire origin of replication or
- the entire ITRs

of said animal adenovirus genome by the homologue sequences of the 5' and 3' ITRs of a human adenovirus genome.

Claim 32. (Previously Presented) A viral preparation obtained according to the method of claim 1, wherein said viral preparation is helper-free.

Claim 33. (Original) A host cell comprising a viral preparation according to claim 32.

Claim 34. (Withdrawn) A pharmaceutical composition comprising a viral preparation according to claim 32.

Claim 35. (Withdrawn) A method for the treatment of disease by gene therapy or immunotherapy comprising administering an effective amount of the viral preparation according to claim 32 to a patient in need of such treatment.

Claim 36. (Previously Presented) The method of claim 1 wherein step (b) is replaced by the step of culturing the cell obtained in step (a) under appropriate conditions to allow the production of viral particles comprising (i).

Claim 37. (Previously Presented) The method of claim 11, wherein said second helper (ii) is defective for E3 function.